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Two-Sided Bounds for Linked Unknown Nonlinear Boundary Conditions of Reaction-Diffusion

V. L. TURNER*† AND W. F. AMES†‡

* *Department of Mathematics, Bethany Nazarene College, Bethany, Oklahoma, 73008; and*
‡ *School of Mathematics, Georgia Institute of Technology, Atlanta, Georgia 30332*

Two enzymes bound at opposite ends of a finite interval affect each other via activation and/or inhibition by their respective products. The local concentrations of the diffusing products, in the vicinity of the other enzyme, determines the rate of production by that enzyme of its product. A mathematical model (cf. Thames and Elster [*J. Theor. Biol.* *59* (1976), 415 427]) consists of linear diffusion equations coupled through unknown and nonlinear boundary conditions. When the (nonlinear) functions describing the boundary conditions have certain monotone properties it is shown that the boundary values can be found iteratively by means of convergent two sided bounds. Some results for reaction chains involving more that two enzymes are presented.

PROBLEM FORMULATION

Problems associated with separated cooperatively coupled enzymes bound to membranes at $x = 0$ and $x = L$ are of considerable interest in various biological areas. The first model examined herein concerns two enzymes that affect each other by activation and/or inhibition. Their respective products diffuse and decay in the region separating the enzyme sites. The local concentration of one product, in the vicinity of the other enzyme, determines the rate of production by that enzyme of its product. In the subsequent analysis we will study the problem formulated by Thames and Elster [1].

Let $u(x, t)$ and $v(x, t)$ represent concentrations of effectors of enzymes $\hat{U}$ and $\hat{V}$ localized at $x = 0$ and $x = L$. The positive parameters D, γ, α and θ are diffusion coefficient, first order decay, flux of u or v from the boundary due to the non-linear responses $F(v)$ and $G(u)$ and the concentration for which half-maximal activation or inhibition occurs, respectively. The resulting reaction diffusion equations are

$$\begin{aligned} u_t &= Du_{xx} - \gamma u, \\ v_t &= Dv_{xx} - \gamma v, \end{aligned} \tag{1}$$

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$0 \leqslant t < \infty, 0 < x < L$, with boundary data ($t > 0$)

$$-Du_x(0, t) = \alpha F[v(0, t)], \qquad u_x(L, t) = 0,$$
$$v_x(0, t) = 0, \qquad Dv_x(L, t) = \alpha G[u(L, t)], \tag{2}$$

and with suitable initial data which is taken to be zero, herein. The functions F and G are known but the boundary functions $v(0, t)$ and $u(L, t)$ are unknown. The constants are assumed to be the same for the effectors $\hat{U}$ and $\hat{V}$ so that a nondimensional formulation can be easily employed.

Upon introducing the transformations $u \to u/\theta$, $v \to v/\theta$, $x \to x/L$, $t \to Dt/L^2$, $q^2 = L^2\gamma/D$, $p = \alpha/\theta(\gamma D)^{1/2}$ *or* $p = \alpha L/\theta D$ the dimensionless equations become

$$\begin{matrix} u_t = u_{xx} - q^2 u \\ v_t = v_{xx} - q^2 v \end{matrix} \quad \text{in} \quad 0 < x < 1, \quad 0 < t < \infty, \tag{3}$$

with boundary data ($t > 0$)

$$-u_x(0, t) = pqF[v(0, t)], \tag{4a}$$
$$u_x(1, t) = 0, \tag{4b}$$
$$v_x(0, t) = 0, \tag{4c}$$
$$v_x(1, t) = pqG[u(1, t)], \tag{4d}$$

and zero inintial data.

Single equations of type (3), without the interconnected boundary conditions, have been studied by Mann and Wolf [2], Roberts and Mann [3], Padmavally [4] and Levinson [5] in the context of radiation heat transfer and superfluidity. An easily accessible source summarizing those papers is the book by Saaty [6]. Several of the proofs are easy extensions of work discussed in Saaty [6]. Consequently, their exposition will be brief.

If the right hand sides of (4a) and (4d) were replaced by known functions of t the solutions could be obtained by Laplace transformation. Substituting for those known functions the right hand sides of (4a) and (4d) the solutions of (3) are

$$v(x, t) = pq \int_0^t \frac{G[u(1, s)]}{[\pi(t - s)]^{1/2}} e^{-q^2(t-s)} \sum_{n=-\infty}^{\infty} \exp\left[-\left(\frac{x}{2} + n + \frac{1}{2}\right)^2 \Big/ (t - s)\right] ds \tag{5}$$

$$u(x, t) = pq \int_0^t \frac{F[v(0, s)]}{[\pi(t - s)]^{1/2}} e^{-q^2(t-s)} \sum_{n=-\infty}^{\infty} \exp\left[-\left(-\frac{x}{2} + n + 1\right)^2 \Big/ (t - s)\right] ds. \tag{6}$$

Since the quantitites $u(1, t)$ and $v(0, t)$ are sought the substitution of $x = 0$ in (5) and $x = 1$ in (6) generates the nonlinear Volterra integral equations

$$U(t) = u(1, t) = pq \int_0^t \frac{F[V(s)]}{[\pi(t-s)]^{1/2}} e^{-q^2(t-s)} \sum_{n=-\infty}^{\infty} \exp\left[-\left(n+\frac{1}{2}\right)^2 \Big/ (t-s)\right] ds \tag{7}$$

and

$$V(t) = v(0, t) = pq \int_0^t \frac{G[U(s)]}{[\pi(t-s)]^{1/2}} e^{-q^2(t-s)} \sum_{n=-\infty}^{\infty} \exp\left[-\left(n+\frac{1}{2}\right)^2 \Big/ (t-s)\right] ds. \tag{8}$$

Equations (7) and (8) clearly display the coupling between the integral equations. Biochemical considerations (see Thames and Elster [1]) dictate the following restrictions on F and G in the inhibitory case: (a) Piecewise continuity; (b) monotonically decreasing; (c) $0 < F \leqslant 1$, $0 < G \leqslant 1$; (d) $\lim_{w\to\infty} F(w) = 0$, $\lim_{w\to\infty} G(w) = 0$. One typical choice for F and G is

$$F(w) = \frac{\theta^2}{\theta^2 + w^2}, \qquad G(w) = \frac{\theta^2}{\theta^2 + w^2}, \qquad \theta > 0.$$

We now examine how the properties of F and G affect the character of an iteration process. The appropriate mathematical theorems are detailed in the next section. In particular we wish to obtain bilateral (two sided) convergent algorithms which have computational use as well as proving existence and uniqueness.

Fundamental Theorems—Inhibitory Case

Equations (7) and (8) are special cases of the system

$$\begin{aligned} u(t) &= \int_0^t f(t, s, v(s))\, ds, \\ v(t) &= \int_0^t g(t, s, u(s))\, ds \end{aligned} \tag{9}$$

so our theorems will be cast in the notation of (9). Extensions to 4 coupled equations will be given later in the paper. The first theorem establishes the importance of the monotone character of f and g to accomplish the bilateral iteration goal since it establishes upper and lower bounds on the solutions.

THEOREM 1. *Let f and g satisfy the following properties:*

(i) $f(t, s, v)$ *and* $g(t, s, u)$ *are defined for* $0 \leqslant s \leqslant t \leqslant T$ *and all real* v *and* u;

(ii) f *and* g *are monotonically decreasing in* v *and* u *for fixed* s *and* t;

(iii) $f(t, s, \phi(s))$ *and* $g(t, s, \phi(s))$ *are absolutely integrable on* $0 \leqslant s \leqslant t$ *for each* t *satisfying* $0 < t \leqslant T$ *and for each function* $\phi(s)$ *continuous on* $0 \leqslant s \leqslant T$;

(iv) $\lim_{t\to 0} \int_0^t f(t, s, \phi(s))\, ds = 0$, $\lim_{t\to 0} \int_0^t g(t, s, \phi(s))\, ds = 0$ *for each such* ϕ *of* (iii).

If $u(t)$ *and* $v(t)$ *are solutions of* (9) *and* $a(t), b(t), c(t)$ *and* $d(t)$ *are continuous on* $[0, T]$ *and satisfy the inequalities*

$$a(t) < \int_0^t f(t, s, d(s))\, ds, \tag{10a}$$

$$b(t) > \int_0^t f(t, s, c(s))\, ds, \tag{10b}$$

$$c(t) < \int_0^t g(t, s, b(s))\, ds, \tag{10c}$$

$$d(t) > \int_0^t g(t, s, a(s))\, ds \tag{10d}$$

for all $t \in [0, T]$, *then*

$$\begin{aligned} a(t) &< u(t) < b(t), \\ c(t) &< v(t) < d(t) \end{aligned} \tag{11}$$

hold on $[0, T]$.

This is an extension of a theorem to be found in Saaty [6, p. 280] so only a brief argument will suffice.

At $t = 0$ it follows from (9) that $u(0) = 0$, $v(0) = 0$. Thus $a(0) < 0 = u(0)$ and $b(0) > 0 = u(0)$ so that $a(0) < u(0) < b(0)$. Similarly $c(0) < v(0) < d(0)$. If the conclusion does not hold on $[0, T]$ then there is a first point $t_0 > 0$ in this closed interval at which at least one inequality does not hold. Let us suppose that $a(t_0) = u(t_0)$. Now $c(t) < v(t) < d(t)$ for $0 \leqslant t < t_0$, so that

$$\begin{aligned} a(t_0) = u(t_0) &= \int_0^{t_0} f(t_0, s, v(s))\, ds \\ &\geqslant \int_0^{t_0} f(t_0, s, d(s))\, ds > a(t_0); \end{aligned}$$

since f is monotonically decreasing and (10a) holds by assumption. The remaining arguments are similar in nature.

On occasion admission of equality in the conclusions of Theorem 1 is useful. The following corollary takes care of this.

COROLLARY 1. *Let f and g satisfy the conditions of Theorem 1 and the Lipschitz condition*

$$\begin{aligned}(\mathrm{v})\quad &|f(t,s,w)-f(t,s,z)| \leqslant L\,|w-z|,\\ &|g(t,s,w)-g(t,s,z)| \leqslant L\,|w-z|.\end{aligned} \tag{12}$$

If equality signs are permitted in (10a–d) *then equality signs are guaranteed in the conclusions* (11).

Once more the argument here is a modest extension of the result in Saaty [6, p. 281] so the proof is omitted.

At this juncture we could study various forms of a general iteration such as

$$u_{n+1} = \int_0^t f(t, s, v_n(s))\,ds, \tag{13a}$$

$$v_{n+1} = \int_0^t g(t, s, u_n(s))\,ds, \tag{13b}$$

or (13a) plus

$$v_{n+1} = \int_0^t g(t, s, u_{n+1}(s))\,ds. \tag{13c}$$

However our major goal concerns the enzyme problem so we will consider it for the general treatment.

ITERATION

Since u, v represent concentrations, they are always nonnegative. However, to utilize Theorem 1 the integrands must be defined for *all* real u and v. To accomplish this define

$$\begin{aligned} F^*(v) &= F(0) \quad \text{if} \quad v < 0 & G^*(u) &= G(0) \quad \text{if} \quad u < 0\\ &= F(v) \quad \text{if} \quad v \geqslant 0; & &= G(u) \quad \text{if} \quad u \geqslant 0\end{aligned} \tag{14}$$

whereupon (7) and (8) become

$$U(t) = \int_0^t F^*(V(s))\,h(t-s)\,ds = (TV)(t), \tag{15a}$$

$$V(t) = \int_0^t G^*(U(s))\,h(t-s)\,ds = (SU)(t). \tag{15b}$$

These integrands are defined for all real V and U and are monotonically decreasing in V and U, respectively. With intial values $U_0(t) = 0$, $V_0(t) = 0$, recursive algorithms are selected as

$$U_{N+1}(t) = (TV_N)(t), \tag{16a}$$

$$V_{N+1}(t) = (SU_N)(t). \tag{16b}$$

Acceleration of convergence can sometimes be achieved by selecting

$$V_{N+1}(t) = (SU_{N+1})(t) \tag{16c}$$

as an alternative to (16b). In what follows (16a, b) will be analyzed but the procedure is the same with (16a, c). But, as we shall see, (16c) is sometimes not a viable alternative. On the other hand (16a) is sometimes not useful.

Because the integrands of (15a–b) are nonnegative and monotonically decreasing in V and U it follows that for every t in $[0, T]$, $U_i \geqslant 0$ and $V_i \geqslant 0$ for all $i = 0, 1, \ldots$. Further, from these two properties, it follows that the iteration is bilateral (two sided). Since $V_2 \geqslant V_0 = 0$, $U_3 = TV_2 \leqslant TV_0 = U_1$. Similarly, $V_3 = SU_2 \leqslant SU_0 = V_1$. Thus $U_3(t) \leqslant U_1(t)$ and $V_3(t) \leqslant V_1(t)$. Now from $U_2 = TV_1$, $U_1 \geqslant U_3 = TV_2$, $V_2 = SU_1$ and $V_1 \geqslant V_3 = SU_2$ it follows from Corollary 1, with $b \to U_1$, $c \to V_2$, $d \to V_1$, $a \to U_2$, that

$$U_2 \leqslant U \leqslant U_1, \qquad V_2 \leqslant V \leqslant V_1, \tag{17}$$

Further $U_3 \leqslant U_1$ implies $SU_3 \geqslant SU_1$ or $V_4 \geqslant V_2$. Also $V_3 \leqslant V_1$ implies $U_4 \geqslant U_2$. Thus, again by the corollary

$$U_2 \leqslant U \leqslant U_3, \qquad V_2 \leqslant V \leqslant V_3$$

so that

$$\begin{aligned} 0 = U_0 &\leqslant U_2 \leqslant U \leqslant U_3 \leqslant U_1 \quad \text{and} \quad U_4 \geqslant U_2, \\ 0 = V_0 &\leqslant V_2 \leqslant V < V_3 \leqslant V_1 \quad \text{and} \quad V_4 \geqslant V_2. \end{aligned}$$

Proceeding in this way it is an easy inductive argument to show that

$$\begin{aligned} U_0 \leqslant U_2 \leqslant \cdots \leqslant U_{2n} \leqslant \cdots \leqslant U \leqslant \cdots \leqslant U_{2n+1} \leqslant \cdots \leqslant U_3 \leqslant U_1, \\ V_0 \leqslant V_2 \leqslant \cdots \leqslant V_{2n} \leqslant \cdots \leqslant V \leqslant \cdots \leqslant V_{2n+1} \leqslant \cdots \leqslant V_3 \leqslant V_1. \end{aligned} \tag{18}$$

The algorithm given by (16) has been established to be two sided. The even (odd) subsequences are monotone increasing (decreasing) and bounded above (below) and therefore converge. It remains to show that the convergence is uniform, on any finite interval, to continuous limit functions which are solutions of the integral equations and to obtain an error estimate for the successive approximations.

THEOREM 2. *The sequences* $\{U_N(t)\}$, $\{V_N(t)\}$ *converge uniformly to continuous limit functions* $U(t)$, $V(t)$, *on any finite interval* $0 \leq t \leq T$, *which are solutions of the integral equations* (7) *and* (8).

Critical to the argument in establishing this result is a good bound on the infinite series in (7) or (8). First we show that

$$\sum_{-\infty}^{\infty} \exp[-(n + \tfrac{1}{2})^2/(t - s)] \leq (1 + k)\,[\pi(t - s)]^{1/2}, \tag{19}$$

where k is to be defined. This result follows from the observation that

$$\sum_{\substack{n=-\infty \\ n\neq 0,-1}}^{\infty} \exp[-(n + \tfrac{1}{2})^2/(t - s)] < \int_{-\infty}^{\infty} \exp[-x^2/(t - s)]\,dx = [\pi(t - s)]^{1/2}$$

since for $n - 1 \leq x \leq n$, $n \neq 0, -1$,

$$\exp[-x^2/(t - s)] > \exp[-(n + \tfrac{1}{2})^2/(t - s)].$$

Finally, choose k so that the excepted terms ($n = 0, -1$) are bounded by $k(\pi(t - s))^{1/2}$. In particular

$$2 \exp\left[-\frac{1}{4(t - s)}\right] < k[\pi(t - s)]^{1/2}$$

if $k \geq (2/\pi)^{1/2} \exp(-\tfrac{1}{2})$.

Using (19) it follows that

$$U_N(t) \leq pq(1 + k) \int_0^t F^*[V_{N-1}(s)]\,ds, \qquad V_N(t) \leq pq(1 + k) \int_0^t G^*[U_{N-1}(s)]\,ds. \tag{20}$$

As a consequence of (20) the inequalities

$$| U_1(t) - U_0(t)| = U_1(t) \leq pq(1 + k) \int_0^t F^*(V_0)\,ds = pq(1 + k)\,F(0)\,t$$

and

$$V_1(t) \leq pq(1 + k)\,G(0)\,t$$

result. By induction it follows that

$$| U_{N+1}(t) - U_N(t)| \leq \frac{[pq(1 + k)\,L]^{N+1}\,F(0)\,t^{N+1}}{L(N + 1)!} \tag{21a}$$

and

$$| V_{N+1}(t) - V_N(t)| \leq \frac{[pq(1 + k)L]^{N+1}\,G(0)\,t^{N+1}}{L(N + 1)!}, \tag{21b}$$

where L is the Lipschitz constant of (12).

The inequalities (21) are sufficient to establish that the sequences $\{U_N(t)\}$ and $\{V_N(t)\}$ converge uniformly to continuous limit functions $U(t)$ and $V(t)$ on any finite interval $0 \leqslant t \leqslant T$. They also provide upper bounds on the error of the approximate solution even though their practical value is limited. The last step in the proof is to demonstrate that the solutions for the modified integral equations, with F^* and G^* instead of F and G, are indeed solutions of the original equations. This is accomplished in exactly the same way as is demonstrated in Saaty [6, p. 284] and is therefore omitted.

For the present dual inhibitory case both F and G are monotonically decreasing functions. For this case, if (16b) is replaced by the accelerated algorithm (16c), contradictory results are obtained. From the definitions $U_1 \geqslant U_0 = 0$ and $V_1 \geqslant V_0 = 0$. But from (16c) $V_1 = SU_1 \leqslant SU_0 = V_0 = 0$ which is contradictory so (16c) cannot be employed with the previous initial choices ($U_0 = 0$, $V_0 = 0$). However, a re-examination of (16a, c) discloses that an initial U_0 *need not be selected.* If this is not done then it is easy to see that the $\{V_N\}$ form an monotone increasing sequence and the $\{U_N\}$ a monotone decreasing sequence bounded below by zero and above by $U_1(t)$. Reversing the roles in (16a, c) — that is employing $V_{N+1}(t) = (SU_N)(t)$ and $U_{N+1}(t) = (TV_{N+1})(t)$ will interchange the properties of the sequences. But in neither case do we obtain the desired two-sided algorithm.

THE ACTIVATION-INHIBITION CASE

The activation-inhibition case differs from the mutual inhibition case in that F of (4a) is monotonically decreasing while G of (4d) is monotonically increasing. In the notation of (9) and the general Theorem 1 this means that f is monotonically decreasing in v and g is monotonically increasing in u. Of course the theorem is no longer valid. But studies of the iteration (13a) and (13b) written as

$$u_{n+1} = Tv_n\,, \qquad v_{n+1} = Su_n \tag{22}$$

and (13a) and (13c) written as

$$u_{n+1} = Tv_n\,, \qquad v_{n+1} = Su_{n+1} \tag{23}$$

or

$$v_{n+1} = Su_n\,, \qquad u_{n+1} = Tv_{n+1} \tag{23'}$$

are particularly interesting. Here the operator T is *antitone* ($w_0 < w_1$ implies $Tw_0 > Tw_1$) and S is *syntone* ($w_0 < w_1$ implies $Sw_0 < Sw_1$).

With T antitone and S syntone the iterates that result from (22), with $U_0 = 0$, $V_0 = 0$, have the *paired* alternating form

$$u_0 < u_3 < u_4 < u_7 < u_8 < \cdots \qquad \cdots < u_6 < u_5 < u_2 < u_1\,,$$
$$v_0 < v_1 < v_4 < v_5 < \cdots \qquad \cdots < v_7 < v_6 < v_3 < v_2$$

which continues in this pattern. However, we are unable to establish uniqueness by the theorems of the preceding section. If this iteration is employed an estimate of the error can be obtained by examining the difference of appropriate upper and lower bounds.

As an alternative to (22) the iterates of (23′), or (23), deliver alternative sequences for the activation-inhibition case! Thus with T antitone and S syntone the iterates of (23′), with $u_0 = 0$, have the form

$$0 = u_0 < u_2 < u_4 < \cdots < u_{2n} < \cdots < u_{2n+1} < \cdots < u_3 < u_1 ,$$
$$v_1 < v_3 < \cdots < v_{2n-1} < \cdots < v_{2n} < \cdots < v_4 < v_2 .$$

So in the activation-inhibition case this iteration is preferred.

The Activation-Activation Case

For the mutual activation case both F and G are monotonically increasing. A typical example is given by

$$F(w) = \frac{w^2}{\theta^2 + w^2} .$$

In the general case, (13), this means that both T and S are syntone and hence the algorithms generate monotone iterates rather than two sided ones.

An Extension—A Four Enzyme Case

Consider the case of four enzymes, two ($\hat{U}$ and $\hat{W}$) at $x = 0$ and two ($\hat{V}$ and $\hat{Y}$) at $x = 1$. If $\hat{U}$ activates $\hat{V}$, $\hat{V}$ inhibits $\hat{W}$, $\hat{W}$ activates $\hat{Y}$ and $\hat{Y}$ inhibits $\hat{U}$ the model equations for the effectors are

$$\begin{aligned} u_t - u_{xx} &= -q^2 u, & v_t - v_{xx} &= -q^2 v, \\ w_t - w_{xx} &= -q^2 w, & y_t - y_{xx} &= -q^2 y \end{aligned} \tag{24}$$

with boundary conditions

$$\begin{aligned} u_x(1, t) = 0, \qquad v_x(0, t) &= 0, \qquad w_x(1, t) = 0, \qquad y_x(0, t) = 0 \\ -u_x(0, t) = pqF[y(0, t)], &\qquad v_x(1, t) = pqG[u(1, t)], \\ -w_x(0, t) = pqH[v(0, t)], &\qquad y_x(1, t) = pqK[w(1, t)], \end{aligned} \tag{25}$$

and zero initial conditions. The functions $F(y)$ and $H(v)$ are monotonically decreasing, while $G(u)$ and $K(w)$ are monotonically increasing. After Laplace transforming in time, solving, inverting and setting $x = 0$ the ***unknown boundary conditions*** $u(1, t) = U(t)$, $v(0, t) = V(t)$, $w(1, t) = W(t)$ and $y(0, t) = Y(t)$ are determinable from the coupled integral equations (generalizations for (7) and (8)), in iterative form,

$$\begin{aligned} U_{N+1}(t) &= T_F Y_N(t), \\ V_{N+1}(t) &= T_G U_N(t), \\ W_{N+1}(t) &= T_H V_N(t), \\ Y_{N+1}(t) &= T_K W_N(t), \end{aligned} \tag{26}$$

with

$$U_0 = V_0 = W_0 = Y_0 = 0.$$

The operators T_F and T_H are antitone and T_G and T_K are syntone. A detailed study of the iteration produces the *paired alternating* form analogous to that of the activation-inhibition case. Specifically we find

$$U_0 < U_3 < U_4 < U_7 > U_8 \cdots < U_6 < U_5 < U_2 < U_1$$

and similarly for $\{W_N\}$, while

$$V_0 < V_1 < V_4 < V_5 < V_8 < V_9 < \cdots < V_7 < V_6 < V_3 < V_2$$

and similarly for $\{Y_N\}$.

Remark. The iteration (22), with T antitone and S syntone can be composed into

$$u_{n+2}(t) = T(Su_n)(t),$$

where the composed operator TS is antitone. This suggests that paired alternating iterates will occur. We can study (26) in the same way.

On the other hand (23) can be composed into

$$u_{n+1}(t) = Tv_n = T(Su_n)(t),$$

where the composed operator TS is antitone. Thus alternating iterates are sure to occur.

Example Computations

In what follows we shall assume that F and G of (7) and (8) have exactly the same form. As a consequence only the single equation

$$U(t) = \int_0^t F[U(s)]\, h(t - s)\, ds \tag{27}$$

needs consideration.

EXAMPLE 1. With

$$F[U] = 1 \qquad U \leqslant 1$$
$$\quad 0 \qquad U > 1 \tag{28}$$

the "iteration" becomes

$$U_1(t) = \int_0^t h(t-s)\, ds,$$

where what is desired is the smallest positive value of t, say t_0, such that $U_1 = 1$. Then

$$\begin{aligned} U(t) = U_2(t) &= U_1(t), && t \leqslant t_0 \\ &= U_1(t_0) = 1, && t > t_0 \end{aligned}$$

is the desired solution.

This calculation was carried out with the quadratic rule for those values of p and q shown in Table I. The function $U(t)$ is given in Figure 1 for $p = 100$ and $q = 1$.

TABLE I

p	q	t_0
100	0.1	.2495
100	1	.10945
500	4	.0651

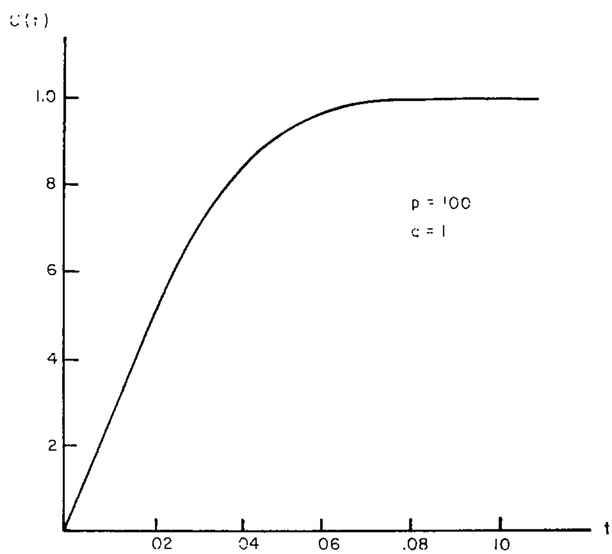

FIGURE 1

EXAMPLE 2. Here the function

$$F[U] = \frac{1}{1 + U^2} \tag{29}$$

is selected. Then the iteration takes the form

$$U_n(t) = \int_0^t F[U_{n-1}(s)]\, h(t-s)\, ds$$

whose calculation is hampered by the need for many intermediate values of $U_{n-1}(s)$ in order to carry out the numerical integration. To eliminate this complexity of additional computation and storage requirements we developed the following iterative sequence of upper and lower bounds, denoted respectively by $\bar{U}_k$ and $\underline{U}_k$ for all $k = 1, 2, \ldots$ and $j = 1, 2, \ldots, J$:

$$\underline{U}_1(t_j) = 0 \qquad \text{for all } j$$

$$\bar{U}_{2n}(t_j) = \sum_{k=1}^{j} \int_{t_{k-1}}^{t_k} F[\underline{U}^*_{2n-1,k}(s)]\, h(t_j - s)\, ds$$

$$\underline{U}^*_{2n-1,k}(s) = \frac{\underline{U}_{2n-1}(t_k) - \underline{U}_{2n-1}(t_{k-1})}{t_k - t_{k-1}}(s - t_{k-1}) + \underline{U}_{2n-1}(t_{k-1})$$

$$\underline{U}_{2n+1}(t_j) = \sum_{k=1}^{j} F[\bar{U}_{2n}(t_k)] \int_{t_{k-1}}^{t_k} h(t_j - s)\, ds$$

During the calculation use is made of the following information: $t_0 = 0$, $\underline{U}_{2n-1}(0) = 0$ for all $n \geqslant 1$, and $\lim_{s \to t} h(t-s) = 0$. Convergence of this iteration is easily established in a manner similar to that previously discussed. In actual calculation, convergence to five significant figures had already occurred after four to six iterations.

For $p = 100$, $q = 0.1$ a few of the rounded converged bounds are shown in Table II.

The loss of accuracy is due to the accumulation of numerical error and our requirement of five significant figure accuracy.

TABLE II

t	0.125	0.175	0.225	0.250
$\underline{U}$	0.16962	0.44171	0.79083	0.97697
$\bar{U}$	0.16965	0.44197	0.79463	0.98504

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